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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/060,301	02/01/2002	Yusuke Nakamura	1254-0195P	7091

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EXAMINER	
KIM, YOUNG J	
ART UNIT	**PAPER NUMBER**
1637	

DATE MAILED: 10/22/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/060,301	NAKAMURA ET AL.	
	Examin r	Art Unit	
	Young J. Kim	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-5 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-5 is/are rejected.

7)☒ Claim(s) 1 is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on 01 February 2002 is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☒ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Oath/Declaration

Applicants are advised that the oath is missing two of the inventor's signatures. The signatures of Toshihiro Tanaka and Yozo Onishi are missing.

Drawings

The drawings filed on February 1, 2002 is acceptable.

Priority

Applicant cannot rely upon the foreign priority papers to overcome this rejection because a translation of said papers has not been made of record in accordance with 37 CFR 1.55. See MPEP § 201.15.

Claim Objections

Claim 1 is objected to because of the following informalities: Claim 1 recites the phrase, "typing for distinguishing the site(s) of single nucleotide polymorphism of nucleotides contained in a plurality of nucleotide sequences amplified in the above amplification step ***using the amplified nucleotide sequences***." The bolded phrase is redundant and not necessary because the phrase already makes clear that the nucleotide sequences amplified in the above amplification step is being used. Appropriate correction is required.

Claim 2 appears to contain a grammatical error. For example, the phrase, "amplifying employs the polymerase chain reaction," should be "amplifying employs ***a*** polymerase chain reaction."

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-5 are rejected under 35 U.S.C. 102(a) as being anticipated by Ohnishi et al. (Journal of Human Genetics, August 2001, vol. 46, no. 8, pages 471-477).

Preliminarily, the inventive entity of the instant application differs from that to the applied reference.

Ohnishi et al. disclose a method of detecting SNP by simulataneously amplifying a plurality of nucleotide sequences comprising 100 genomic DNA fragments (Abstract, page 472, 1st column; claim limitation 1), wherein the detection was achieved via Invader assay (Abstract, page 472, 1st column; claim limitation 4). Ohnishi et al. disclose that 40 ng of genomic DNA was used for the method (page 472, 1st column; claim limitation 5), wherein up to 100 pairs of primers were used for amplification (page 472, bottom; claim limitation 3). Although Ohnishi et al. do not explicitly state that a "hot start" procedure was employed for the amplification process, the artisans used a Taqstart™ antibody for the amplification method, which is known to be used

for "hot starting" an amplification reaction (also evidenced by attached product description from BD Biosiences, also available through www.bdbiosciences.com).

Therefore, the invention as claimed is obvious over the cited reference.

Claims 1 and 5 rejected under 35 U.S.C. 102(b) as being anticipated by Wang et al. (Science, May 1998, vol. 280, pages 1077-1082).

Wang et al. disclose a method of SNP genotyping which involves multiplex amplification from a genomic DNA via plurality of primers (pp. 1080). The amplified products are then hybridized on to a microarray comprising a plurality of complementary probes for SNP typing (pp. 1080, 1st column; claim limitation 1). Wang et al. multiplexes 46 loci from a genomic DNA (pp. 1080, 3rd column).

Though Wang et al. do not explicitly disclose the amount of genomic DNA used in the multiplex process, according to *In re Best* 195 USPQ 430, 1997, the court stated that, "Patent Office can require applicant to prove that prior art products do not necessarily or inherently posses characteristics of his claimed product wherein claimed and prior art products are identical or substantially identical, or are produced by identical or substantially identical processes; burden of proof is on applicant" (pp. 430). Since Wang et al. disclose that a substantial amount of loci (therefore use of different primers) were multiplexed, absent evidence to the contrary, it is determined that the amount of genomic DNA used in the process is considered to be inherent property of the disclosure.

Claims 1, 2, and 4 are rejected under 35 U.S.C. 102(b) as being anticipated by Walburger et al. (Mutation Research, January 2001, vol. 432, pages 69-78).

Walburger et al. disclose a TaqMan™ real-time PCR assay for identifying single nucleotide polymorphisms from genomic DNA (page 70, 2nd column, *Materials and Methods*), which involves amplification of two codons, namely codon 63 and codon 63 (therefore simultaneously amplifying a plurality of nucleotide sequences comprising at least one or more SNP) (page 71, *2.6 Real time PCR*; claim limitation 1 and 4). Walburger et al. employs JumpStart™ *Taq* polymerase which is known in the art (as evidenced by the attached product description available through http://www.sigma-origins.co.uk/pdfs/backissues/1047998072.pdf) as being used in a hot start amplification (page 71, *2.6 Real time PCR*; claim limitation 2).

Therefore, Walburger et al. anticipate the invention as claimed.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 2 and 3 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wang et al. (Science, May 1998, vol. 280, pages 1077-1082) in view of Brooks (US 2001/0046670 A1, issued November 29, 2001, priority October 7, 1999).

Wang et al. disclose a mehtod of SNP genotyping which involves multiplex amplification from a genomic DNA via plurality of primers (pp. 1080). The amplified products are then hybridized on to a microarray comprising a plurality of complementary probes for SNP typing

(pp. 1080, 1st column; claim limitation 1). Wang et al. multiplexes 46 loci from a genomic DNA (pp. 1080, 3rd column).

The multiplex amplification of Wang et al. do not use 50 or more primers.

The multiplex amplification of Wang et al. do not employ "hot start" amplification.

Brook discloses a multiplex amplification [0076] reaction which involves hot start amplification [0066].

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the teachings of Wang et al. with the advantage offered by Petrik to arrive at the invention as claimed for the following reasons.

As stated above, although the multiplex amplification of Wang et al. do not employ 50 or more primers, Wang et al. employs multiplex amplification which amplified 46 different loci (page 1080, 3rd column), which equates to 46 primer pairs. Additionally, Wang et al. clearly suggest the advantage of multiplexing more targets:

"We next sought to decrease substantially the sample preparation required to genotype large numbers of SNPs, as required to perform a genomic scan. We developed a protocol based on multiplex PCR in which primer pairs from many different loci are combined in a single reaction." (page 1080, 3rd column).

Therefore, with the above suggestion, one of ordinary skill in the art at the time the invention was made would have been motivated to increase the number of different amplifiable targets through multiplex amplification for the advantage of reducing sample preparation time.

With regard to the hot start amplification process, the advantage for incorporating this teaching is also clearly stated by Brook:

"...other 'Hot Start' type PCR conditions are used to limit primer dimmer artifacts as much as possible." [0066].

As one of ordinary skill in the art in the art of amplification would recognize that primer dimmer artifacts are to be minimized in amplification procedures, it would have been obvious to implement this teachings into the teachings of Wang et al. to arrive at the claimed invention with a reasonable expectation of success.

Claim 3 is rejected under 35 U.S.C. 103(a) as being unpatentable over Walburger et al. (Mutation Research, January 2001, vol. 432, pages 69-78) in view of Wang et al. (Science, May 1998, vol. 280, pages 1077-1082).

Walburger et al. disclose a TaqMan™ real-time PCR assay for identifying single nucleotide polymorphisms from genomic DNA (page 70, 2nd column, *Materials and Methods*), which involves amplification of two codons, namely codon 63 and codon 63 (therefore simultaneously amplifying a plurality of nucleotide sequences comprising at least one or more SNP) (page 71, *2.6 Real time PCR*). Walburger et al. employs JumpStart™ *Taq* polymerase which is known in the art (as evidenced by the attached product description available through http://www.sigma-origins.co.uk/pdfs/backissues/1047998072.pdf) as being used in a hot start amplification (page 71, *2.6 Real time PCR*).

Walburger et al. do not employ more than 50 pairs or more primers in the amplification step.

Wang et al. employs multiplex amplification which amplified 46 different loci (page 1080, 3rd column), which equates to 46 primer pairs.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the teachings of Walburger et al. with the motivation provided by Wang et al. to arrive at the invention as claimed.

Wang et al. clearly disclose the advantage of multiplexing more targets in a PCR assay:

> "We next sought to decrease substantially the sample preparation required to genotype large numbers of SNPs, as required to perform a genomic scan. We developed a protocol based on multiplex PCR in which primer pairs from many different loci are combined in a single reaction." (page 1080, 3rd column).

As one of ordinary skill in the art would recognize such advantage of multiplexing a PCR reaction, with the above suggestion, the artisan, at the time the invention was made, would have been motivated to arrive at the claimed method which increases the number of different amplifiable targets through multiplex amplification for the advantage of reducing sample preparation time with a reasonable expectation of success.

Conclusion

No claims are allowed.

Inquiries

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Young J. Kim whose telephone number is (703) 308-9348. The Examiner can normally be reached from 8:30 a.m. to 7:00 p.m. Monday through Thursday. If attempts to reach the Examiner by telephone are unsuccessful, the Primary Examiner in charge of the prosecution, Dr. Kenneth Horlick, can be reached at (703)-308-3905. If the attempts to reach the above Examiners are unsuccessful, the Examiner's supervisor, Gary Benzion, can be reached at (703) 308-1119. Papers related to this application may be submitted to Art Unit 1637 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 CFR 1.6(d)). NOTE: If applicant does submit a paper by FAX, the original copy should be retained by applicant

or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED, so as to avoid the processing of duplicate papers in the Office. All official documents must be sent to the Official Tech Center Fax number: (703) 872-9306. For Unofficial documents, faxes can be sent directly to the Examiner at (703) 746-3172. Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Young J. Kim

10/17/03

KENNETH R. HORLICK, PH.D
PRIMARY EXAMINER

10/20/03